8. Malignant Disease and Immunosuppression

Contents

Key

R	**Red drug** see GMMMG RAG list *Click on the symbols to access this list*
A	**Amber drug** see GMMMG RAG list *Click on the symbols to access this list*
Gn	**Green drug** see GMMMG RAG list *Click on the symbols to access this list*
U	**If a medicine is unlicensed this should be highlighted in the template as follows** **Drug name** U
	Not Recommended
OTC	**Over the Counter** In line with NHS England guidance, GM do not routinely support prescribing for conditions which are self-limiting or amenable to self-care. For further details see GM commissioning statement.
Order of Drug Choice	Where there is no preferred 1st line agent provided, the drug choice appears in alphabetical order.

Chapter	**8 Malignant Disease and Immunosuppression**
Section	**8.1 Cytotoxic Drugs**
	The chemotherapy of cancer is complex and should be confined to specialists in oncology and haematology. NPSA anti-cancer drug recommendations NOTE: a number of cytotoxic medicines that are used for indications other than cancer are listed elsewhere in this formulary under the relevant chapter e.g. methotrexate for rheumatological indications in chapter 10. Only trained pharmacy personnel should reconstitute cytotoxics and prescription validation should only be carried out by suitably trained pharmacists. Pharmacy Guidelines for the safe use of oral anti-cancer medicines are available on the GMMMG website. The GMCCN policy and procedure for chemotherapy administration provides further information. **All anti-cancer drugs with a positive NICE Health Technology Appraisal are approved for use in Greater Manchester, with a RED RAG status.** NHS England's Cancer Drug Fund provides a further list of approved uses of cytotoxic drugs and the latest national funding policies.
Additional Notes	**Link to additional notes document**
Subsections	**8.1.1 Alkylating drugs, 8.1.2 Anthracyclines and other cytotoxic antibiotics, 8.1.3 Antimetabolites, 8.1.4 Vinca alkaloids and etoposide, 8.1.5 Other antineoplastic drugs**

Additional Notes

All cytotoxics with a positive NICE Health Technology Appraisal are approved for use in Greater Manchester, with a RED RAG status.
NHS England's Cancer Drug Fund provides a further list of approved uses of cytotoxic drugs and the latest national funding policies.

Links to NICE guidance:

Index of NICE guidance on cancer

Links to MHRA advice:

MHRA DSU (April 2017): Ponatinib (Iclusig▼): risk of vascular occlusive events—updated advice on possible dose reduction
MHRA DSU (May 2016): BCR-ABL tyrosine kinase inhibitors: risk of hepatitis B reactivation

MHRA DSU (May 2016): Idelalisib (Zydelig): interim measures following signal of serious infection and deaths related to infection found in clinical trials

MHRA DSU (Sept 2016): Idelalisib (Zydelig▼): updated indications and advice on minimising the risk of infection

Section	**8.2 Drugs affecting the immune response**	
Subsection	**8.2.1 Antiproliferative immunosuppressant**	
First choice	**Azathioprine** Tablets 25mg, 50mg	A Shared care protocols available for: - IBD in adults - IBD in paediatrics - Rheumatological conditions in adults - Dermatology in adults - Neurological conditions in adults - Interstitial lung disease in adults - Autoimmune hepatitis in adults
Alternatives	**Mycophenolate mofetil** Capsules 250mg, Tablets 500mg	A MHRA DSU: Mycophenolate mofetil, mycophenolic acid: new pregnancy-prevention advice for women and men 2015 NICE TA481: Immunosuppressive therapy for kidney transplant in adults NICE TA482: Immunosuppressive therapy for kidney transplant in children and young people
	Mycophenolic acid (Myfortic®) Gastro-resistant tablets 180mg, 360mg	A
Additional notes All new patients commenced on mycophenolate mofetil should be commenced on a "branded generic" preparation. Mycophenolate mofetil and mycophenolic acid are not interchangeable. Patients on Myfortic® must remain on Myfortic®.		
Subsection	**8.2.2 Corticosteroids and immunosuppressants**	
First choice	**Ciclosporin** Capsules 25mg, 50mg, 100mg Oral solution 100mg/ml	A Prescribe by brand. Do not switch between brands.
Alternatives	**Tacrolimus** Capsules 500microgram, 1mg, 2mg, 5mg Granules 200microgram, 1mg Modified-release capsules 500microgram, 1mg, 3mg, 5mg	A MHRA DSU: Oral tacrolimus products: prescribe and dispense by brand name only, to minimise the risk of inadvertent switching between products, which has been associated with reports of toxicity and graft rejection, November 2017
	Sirolimus Tablets 500microgram, 1mg, 2mg Oral solution 1mg/ml	A

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	Basiliximab Powder and solvent for solution for injection 10mg, 20mg	(R) Specialist use only NICE TA481: Immunosuppressive therapy for kidney transplant in adults NICE TA482: Immunosuppressive therapy for kidney transplant in children and young people

Additional notes

Sirolimus tablets (Rapamune®) – the 500microgram tablets are not bioequivalent with the 1mg and 2mg tablets and multiples must not be used as a substitute for the other tablet strengths.

There are 3 different oral formulations of tacrolimus:

- *Adoport*®, *Prograf*®, *Capexion*®, *Tacni*®, and *Vivadex*® are immediate-release capsules that are taken twice daily, once in the morning and once in the evening;
- *Modigraf*® granules are used to prepare an immediate-release oral suspension which is taken twice daily, once in the morning and once in the evening;
- *Advagraf*® is a prolonged-release capsule that is taken once daily in the morning.

Switching between different oral formulations of tacrolimus requires careful supervision and therapeutic monitoring by an appropriate specialist.

Subsection	**8.2.3 Antilymphocyte monoclonal antibodies**	
	Alemtuzumab ▼ Concentrate for IV infusion	(R) Specialist use only Causes lysis of B lymphocytes NICE TA312: Alemtuzumab for treating relapsing-remitting multiple sclerosis
	Natalizumab ▼ Concentrate for solution for infusion 300mg/15ml	(R) Specialist use only MHRA DSU: Natalizumab (Tysabri): progressive multifocal leukoencephalopathy – updated advice to support early detection (April 2016) NICE TA127: Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis
	Ocrelizumab ▼ Concentrate for solution for infusion 300mg/10ml	(R) Specialist use only NICE TA533: Ocrelizumab for treating relapsing–remitting multiple sclerosis
	Ofatumumab ▼ 20 mg solution for injection in pre-filled pen	(R) Specialist use only NICE TA699: Ofatumumab for treating relapsing multiple sclerosis

Subsection	8.2.4 Other immune-modulating drugs	
Interferon Alfa		
	Interferon alfa-2b (rbe) IntronA® Solution for injection (for subcutaneous injection or intravenous infusion) Solution for injection pen (for SC injection)	R
	Interferon alfa-2a (rbe) Roferon-A® Solution for injection pre-filled syringes (for subcutaneous use) Solution for injection cartridges (for *Roferon*® pen device, subcutaneous and intramuscular use) Solution for injection vials (for subcutaneous and intramuscular use)	R
Peginterferon Alfa		
	Peginterferon alfa-2a (rbe) Pegasys® Solution for injection pre-filled syringe (for subcutaneous injection)	R
	Peginterferon alfa-2b (rbe) ViraferonPeg® Powder and solvent for solution for injection pre-filled pen (for subcutaneous injection)	R NICE TA75: peginterferon alfa, interferon alfa, and ribavirin for chronic hepatitis C NICE TA300: peginterferon alfa and ribavirin for treating chronic hepatitis C in children and young people
Interferon Beta		
	Interferon beta–1a Avonex®, Rebif® Solution for injection pre-filled syringe Solution for injection pre-filled pens Powder and solvent for solution for injection vials Solution for injection cartridges (for RebiSmart® device)	R NICE TA527: Beta interferons and glatiramer acetate for treating multiple sclerosis MHRA DSU: Interferon beta: risk of thrombotic microangiopathy and risk of nephrotic syndrome, Oct 2014
	Interferon beta–1b Betaferon® Powder and solvent for solution for injection	R NICE TA527: Beta interferons and glatiramer acetate for treating multiple sclerosis MHRA DSU: Interferon beta: risk of thrombotic microangiopathy and risk of nephrotic syndrome, Oct 2014
Peginterferon beta		
	Peginterferon beta-1a Plegridy® Solution for injection pre-filled pen (for subcutaneous injection)	R

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		NICE TA624: Peginterferon beta-1a for treating relapsing–remitting multiple sclerosis

Additional notes

See also:

- NHS England Specialised commissioning policies for neurology, including disease-modifying therapies for patients with multiple sclerosis
- NICE NG220: Multiple sclerosis in adults: management

	Canakinumab Powder for solution for injection vial 150mg	Ⓡ Specialist use only
	Cladribine Mavenclad® Tablets 10mg	Ⓡ NICE TA616: Cladribine for treating relapsing-remitting multiple sclerosis MHRA DSU: Cladribine (Mavenclad): new advice to minimise risk of serious liver injury
	Dimethyl fumarate Capsules 120mg and 240mg	Ⓡ Specialist use only NICE TA320: Dimethyl fumarate for treating relapsing-remitting MS MHRA DSU: Dimethyl fumarate (Tecfidera®): fatal PML in an MS patient with severe prolonged lymphopenia, March 2015 MHRA DSU: Dimethyl fumarate (Tecfidera): updated advice on risk of progressive multifocal leukoencephalopathy (April 2016) MHRA DSU: Dimethyl fumarate (Tecfidera): updated advice on the risk of progressive multifocal leukoencephalopathy (PML) associated with mild lymphopenia, Jan 2021
	Diroximel fumarate Gastro-resistant capsules 231mg	Ⓡ NICE TA794: diroximel fumarate for treating relapsing–remitting multiple sclerosis
	Fingolimod ▼ Capsules 500microgram	Ⓡ MHRA DSUs: • Fingolimod (Gilenya▼): updated advice about the risks of serious liver injury and herpes meningoencephalitis, Jan 2021 • Fingolimod (Gilenya▼): increased risk of congenital malformations; new contraindication during pregnancy and in women of childbearing potential not using effective contraception, Sept 2019 • Fingolimod (Gilenya▼): updated advice about risk of cancers and serious infections, Dec 2017 • Fingolimod (Gilenya▼) new contraindications for patients with pre-existing cardiac disorders, Dec 2017

		• MS therapies: signal of rebound effect after stopping or switching therapy, April 2017 • Fingolimod (Gilenya▼): risks of progressive multifocal leukoencephalopathy, basal-cell carcinoma, and opportunistic infections (April 2016) • Bradycardia and heart block, Jan 2013 • Fingolimod: not recommended for patients at known risk for cardiovascular adverse events, May 2012 • NICE TA254: Fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis
	Glatiramer acetate Copaxone® Solution for injection pre-filled syringe 20mg/ml	R NICE TA527: Beta interferons and glatiramer acetate for treating multiple sclerosis
	Ponesimod ▼ Tablets	R NICE TA5767: Ponesimod for treating relapsing–remitting multiple sclerosis
	Siponimod ▼ Tablets 0.25 mg and 2 mg	R NICE TA656: Siponimod for treating secondary progressive multiple sclerosis
Additional notes See also NHS England Specialised Commissioning policies for Neurosciences, including Treatment Algorithm for Multiple Sclerosis Disease-Modifying Therapies.		

Section	**8.3 Sex hormones and hormone antagonists in malignant disease**	
Subsection	**8.3.1 Oestrogens**	
	Diethylstilbestrol Tablets 1mg, 5mg **Ethinylestradiol** Tablets 10microgram, 50microgram, 1mg	Gn following specialist initiation
Subsection	**8.3.2 Progestogens**	
	Medroxyprogesterone acetate Tablets 10mg, 100mg, 200mg **Megestrol acetate** Tablets 160mg	Gn following specialist initiation
Subsection	**8.3.4 Hormone antagonists**	
Subsection	**8.3.4.1 Breast cancer**	
	Anastrozole Tablets 1mg	Gn following specialist advice
	Exemestane Tablets 25mg	Gn following specialist advice
	Letrozole Tablets 2.5mg	Gn following specialist advice
	Tamoxifen Tablets 10mg, 20mg	Gn following specialist advice
Additional notes NICE TA112 Breast cancer (early) - hormonal treatments		
Subsection	**8.3.4.2 Gonadorelin analogues and gonadotrophin-releasing hormone antagonists**	
Gonadorelin analogues		
	Goserelin Zoladex® Implant pre-filled syringe 3.6mg (four weeks) Implant pre-filled syringe 10.8mg (twelve weeks)	A (for licensed indications) GMMMG SCPs: • GnRH analogues for breast cancer in adults • Goserelin (Zoladex), Leuprorelin (Prostap) or Triptorelin (Decapeptyl SR) in the treatment of prostate cancer in adults • GnRH analogues for patients aged 17 years or over under Indigo Gender Service

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	Leuprorelin Prostap® Suspension for injection pre-filled syringe 3.75mg (four weeks) Suspension for injection pre-filled syringe 11.25mg (three months)	A (for licensed indications) GMMMG SCPs: • GnRH analogues for breast cancer in adults • Goserelin (Zoladex), Leuprorelin (Prostap) or Triptorelin (Decapeptyl SR) in the treatment of prostate cancer in adults • GnRH analogues for patients aged 17 years or over under Indigo Gender Service
	Triptorelin Decapeptyl® Suspension for injection vials 3mg (every four weeks) Suspension for injection vials 11.25mg (every three months) Suspension for injection vials 22.5mg (every six months) **Triptorelin** Gonapeptyl® Suspension for injection pre-filled devices 3.75mg (every four weeks)	A (for licensed indications) GMMMG SCP: Goserelin (Zoladex), Leuprorelin (Prostap) or Triptorelin (Decapeptyl SR) in the treatment of prostate cancer in Adults GMMMG SCP: GnRH analogues for patients aged 17 years or over under Indigo Gender Service
Anti-androgens		
	Bicalutamide Tablets 50mg, 150mg **Cyproterone acetate** Tablets 50mg, 100mg	Gn following specialist initiation. NB: unlicensed if used in prostate cancer (metastatic) with the aim of retaining sexual function Gn following specialist initiation
Gonadotrophin-releasing hormone antagonists		
	Degarelix Powder for solution for injection 80mg, 120mg	A TA404: Degarelix for treating advanced hormone-dependent prostate cancer GMMMG SCP: Degarelix in advanced hormone dependent prostate cancer
Additional notes Link to additional notes document		
Subsection	**8.3.4.3 Somatostatin analogues**	
First choice	**Octreotide** Solution for injection (various forms) 50microgram/1ml 100microgram/1ml, 500microgram/1ml, 1mg/5ml	R See HCD commissioning statement

	Suspension for injection (depot) 10mg, 20mg, 30mg	
Alternatives	**Lanreotide** Solution for injection pre-filled syringe 60mg, 90mg, 120mg	Ⓡ
Additional notes		